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Serial No.: 08/822,963  
Filed: March 21, 1997

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### **REMARKS**

Reconsideration of this application is respectfully requested.

Claims 68-90 were previously pending in this application. Claims 68 and 74, 78, 81, 85, 86-87 and 89-90 have been amended. No claims have been added or canceled by this paper. Accordingly, claims 68-90 as amended are presented for further examination on the merits.

In a sincere effort to define their invention more clearly and place the claims in a more allowable condition, Applicants have effected a number of changes to the claims. **First**, the end of claim 68 has been amended to recite "wherein said viral vector nucleic acid comprises at least one non-deletion modification with a non-retroviral sequence, said non-deletion modification leading to a reduction, inhibition or elimination of viral vector function." **Second**, claim 74 has been amended to recite "[t]he vector of claim 68, wherein said non-deletion modification comprises a substitution of a native sequence segment with a non-retroviral sequence segment, said non-retroviral sequence segment not being derived from promoter/enhancer sequences of a retrovirus. Claim 74 previously depended from claim 73, and as was astutely observed by the Examiner, the former language in claim 74 did not limit that of claim 73. **Third**, claim 78 now reads "[t]he vector of claim 68, further comprising a segment of a viral vector terminator or a segment of a processing signal, or both a viral vector terminator and a segment of a processing signal.

**Fourth**, in claim 81, the phrase "a regulatory portion of" has been inserted in front of the word "genes" in order to conform the language with the "promoter/enhancer regions" recited earlier in the claim. The Markush language in claim 81 has also been modified slightly. **Fifth**, the claim dependency recited in the first (providing) step of claim 85 has been changed from "1" to -- 68 --. **Sixth**, claims 86 and 87 have both been amended to recite that the nucleic acid construct has been modified in a promoter/enhancer region (non-native in the case of claim 87) in "either said providing step or said introducing step" of the process of claim 68. **Finally**, the word "modified" in line 2 of each of claims 89 and 90 has been changed to -- introduced --.

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The foregoing amendments to the claims do not constitute the insertion of new matter into the original disclosure; rather, such amendments are believed to comprise subject matter to which Applicants are duly entitled to claim. Moreover, most if not all of the above amendments to the claims have been implemented to meet the Examiner's requirements for claim clarity or to adopt his suggestions. Entry of these amendments is respectfully requested.

#### **Submission of Information Disclosure Statement**

Shortly after filing the instant Amendment, Applicants' undersigned attorney and his paralegal expect to file an Information Disclosure Statement shortly to submit art-related documents which may be of interest or material to the prosecution of this application.

#### **The Rejection Under 35 U.S.C. §102(b)**

Claims 68-81 and 83-84 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Greatbatch et al. (U.S. Patent No. 5,324,643). In the Office Action (page 2), the Examiner stated:

Both applicants and Greatbatch et al. (U.S. Patent 5,324,643, issued 1/28/94, see whole document, particularly Columns 8, 12, 16 and 17) recite vectors (which can be viral or retroviral) which are capable of expressing exogenous nucleic acid sequences in target cells wherein said vector comprises at least one non-deletion modification (i.e. substitution of a polIII promoter which can be from a tRNA gene) with a non-retroviral sequence leading to an alteration of viral vector function and non-native or native terminator sequences. Therefore, Greatbatch et al. teaches the claimed invention.

The anticipation rejection is respectfully traversed.

As indicated in the opening remarks of this paper, the end of claim 68 has been amended to recite "wherein said viral vector nucleic acid comprises at least one non-deletion modification with a non-retroviral sequence, said non-deletion modification leading to a reduction, inhibition or elimination of viral vector function." In contrast to Applicants' invention as set forth in amended claim 68,

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Greatbatch et al. discloses a viral vector in which an *enhancement* of viral vector function is obtained through, for example, the substitution of a polIII promoter from a tRNA gene. Thus, Greatbatch et al. do not disclose or suggest Applicants' claimed material feature wherein a reduction, inhibition or elimination of viral vector function is achieved through a non-deletion modification with a non-retroviral sequence. Accordingly, there is a lack of identity in the materials claimed by Applicants and Greatbatch's disclosure.

In view of the above amendments to claim 68 and the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the anticipation rejection.

#### The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 68-90 stand rejected for indefiniteness under 35 U.S.C. § 112, second paragraph. In the Office Action (pages 3-4), the Examiner stated:

**[1]** Claim 68 (and dependent claims) are vague in the recitation of the phrase "...non-deletion modification with a non-retroviral sequence leading to an alteration or enhancement of viral vector function." since it is unclear what relationship exists between the "non-deletion modification" and the "non-retroviral sequence".

**[2]** Claim 74 is vague in that there is no antecedent basis for the term "the sequence segments" in claim 73. Also, claim 74 is vague in that the claim recites a sequence segment which is "not related" to promoter/enhancer sequences of a retrovirus. It is unclear what is meant by "not related", i.e. does this term mean other retroviral sequences which are not promoter or enhancer sequences or non-retroviral sequences, etc. Also, claim 74 does not further limit the subject matter of claim 73 in that the claim recites a substitution which can be a retroviral sequence as long as it is "not related" to a retrovirus promoter/enhancer sequence.

**[3]** Claim 78 is vague in that there is no antecedent basis for the term "said viral vector terminator" in claim 68.

**[4]** Claim 81 (and dependent claims) is vague in that applicants recite promoter/enhancer regions selected from genes. Promoter/enhancer regions are not genes, but are portions of the regulatory regions of genes.

**[5]** Claim 85 (and dependent claims) are vague in that claim 85 depends from canceled claim 1.

**[6]** Claims 86 and 87 are vague in the recitation of the phrase "wherein said providing step or introducing step" since this phrase

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appears to be out of context with the rest of the claim and is not connected to the other claim language.

**[7]** Claims 89 and 90 are vague in that the claims recite a nucleic acid construct that has been "modified" by means of an episome or by "transient expression". It is unclear how an episome or transient expression can modify a nucleic acid construct.

The indefiniteness rejection is respectfully traversed.

In view of the number of points raised in the above rejection, Applicants' attorney has taken the liberty of inserting bold bracketed numbers before each point in order to ensure that each and every point is thoroughly addressed. The remarks below are directed to the seven points identified by bold bracketed numbers.

**[1]** It is believed that the above amendments to claim 68 clarifies the relationship between the "non-deletion modification" and the "non-retroviral sequence." As discussed earlier in the opening remarks and also in the rejection under 35 U.S.C. §102, claim 68 now ends with the recitation "wherein said viral vector nucleic acid comprises at least one non-deletion modification with a non-retroviral sequence, said non-deletion modification leading to a reduction, inhibition or elimination of viral vector function."

**[2]** As also indicated in the opening remarks of this paper, claim 74 now reads "[t]he vector of claim 68, wherein said non-deletion modification comprises a substitution of a native sequence segment with a non-retroviral sequence segment, said non-retroviral sequence segment not being derived from promoter/enhancer sequences of a retrovirus. The foregoing language in claim 74 is believed to have obviated the antecedent basis issue with respect to "segments" as well as the vagueness issue in regard to the relationship between the "non-retroviral sequence segment" and the "promoter/enhancer sequences of a retrovirus." Moreover, by changing the claim dependency from 73 to 68, claim 74 properly limits the subject matter of the latter claim from which it now depends.

**[3]** The antecedence problem in claim 78 is believed to have been handled by substituting the article "a" for "said" in two occurrences in the claim.

**[4]** The Examiner's position with respect to promoter/enhancer regions being portions of the regulatory regions of genes - and not genes themselves - has been well taken in the case of claim 81. The above amendments to claim 81 adopt the Examiner's position in this regard.

**[5]** In claim 85, the inadvertent reference to claim 1 in the first step has been corrected to recite "claim 68." Thus, claim 85 no longer depends from a canceled claim.

**[6]** As also indicated earlier in this paper, claims 86 and 87 have been amended to recite that wherein either said providing step or said introducing step, the nucleic acid construct has been modified in a promoter/enhancer region [claim 86] or non-native promoter/enhancer region [claim 87]. The foregoing language in claims 86 and 87 is believed to place both claims in conformance with the process steps of claim 85 from which both claims depend.

**[7]** With respect to the issue in claims 89 and 90 involving the terms "episome" and "transient expression," the substitution of "introduced" for "modified" is believed to have obviated this ground of rejection.

In view of the foregoing remarks and above amendments to the claims, Applicants respectfully request reconsideration and withdrawal of the indefiniteness rejection, thereby placing each of claims 68-90 in an allowable condition.

Favorable action on this application is respectfully requested.

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**SUMMARY AND CONCLUSIONS**

Claims 68-90 are presented for examination in this application. Nine claims have been amended, and no claims have been added or canceled by this paper.

This Amendment is accompanied by a Request For An Extension Of Time (3 months) and a Notice of Appeal To The Board Of Patent Appeals And Interferences, and authorization for the fees therefor. No other fee or fees are believed due in connection with this filing or the documents. In the event that any such other fee or fees are due, however, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If it would be helpful to expediting prosecution of this application, Applicants' undersigned attorney may be contacted during normal daytime business hours at (212) 583-0100, or by facsimile, at (212) 583-0150.

Respectfully submitted,



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